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Research Highlights

Advances in Andrology and Stone Disease

Results from the TRAVERSE trial

This month's column features research advances in the fields of Andrology and Stone Disease. Lincoff et al. reported results from the TRAVERSE trial that explored the safety of testosterone replacement therapy among men who had pre-existing cardiac disease or were at high risk for cardiovascular events. The trial was organised in response to a 2015 US Federal Drug Administration guidance memorandum that required pharmaceutical companies selling testosterone products to evaluate whether these drugs increased the risk of cardiovascular disease. The trial population consisted of men aged 45–80 years with a history of cardiovascular disease or were at high risk of developing cardiac disease. They also had one or more symptoms of hypogonadism including decreased sexual desire or libido, decreased spontaneous erections, fatigue or decreased energy, low or depressed mood, hot flashes or loss of pubic or axillary body hair. All participants had two morning fasting testosterone levels less than 300 ng/dL.

The trial enrolled 5246 men randomized 1:1 to receive testosterone or placebo gel. For those men receiving testosterone the dose was adjusted to maintain serum levels between 350 and 750 ng/dL. The primary metric was the occurrence of a cardiac associated death, a non-lethal myocardial infarction, or a non-fatal stroke. The mean duration of treatment was 22 months and the mean follow up was 33 months. Cardiac events occurred in 182 (7.0%) of the men taking testosterone and 190 (7.3%) taking placebo (HR 0.96 95% CI 0.78–1.17; $P < 0.001$). The trial was designed as a non-inferiority study and clearly showed that testosterone supplements did not increase the likelihood of a cardiovascular event among men with cardiac disease.

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Lincoff AM, Bhasin S, Flavaris P et al. Cardiovascular safety of testosterone replacement therapy. N Eng J Med 2023; https://doi.org/10.1056/NEJMoa2215025.

"Testosterone supplements did not increase the likelihood of a cardiovascular event among men with cardiac disease"

Hydrochlorothiazide for prevention of renal calculi

Dhayat et al. reported results from a landmark trial concerning the use of hydrochlorothiazide (HCTZ) as a treatment to prevent renal calculi. The study was conducted in multiple hospitals throughout Switzerland to evaluate the efficacy of this practice. Researchers enrolled 416 patients with a history of calcium containing kidney stone disease in a double-blind randomized trial. Patients received 12.5 mg, 25 mg, or 50 mg of HCTZ once daily or placebo and were followed for a median 2.9 years. The primary endpoint was a composite of symptomatic or radiographic recurrence of kidney stones. Stone recurrence was found in 60 of the 102 (59%) patients on placebo, 62 of the 105 (59%) taking 12.5 mg HCTZ, 61 of 108 (56%) taking 25 mg HCTZ and 49 of 101 (49%) taking 50 mg HCTZ. All confidence intervals crossed 1.0. There was no relationship between HCTZ dose and the recurrence of kidney stones ($P = 0.66$). Hypokalaemia, gout, new-onset diabetes mellitus, skin allergies and a plasma creatinine exceeding 150% of baseline was more common among patients receiving HCTZ than among those patients receiving placebo.

Dhayat NA, Bonny O, Roth B et al. Hydrochlorothiazide and the prevention of kidney stone recurrence. N Eng J Med 2023; 388: 781–91.

Hydroxycitric acid to facilitate extracorporeal shock wave lithotripsy

Del Carmen Cano Garcia et al. from Spain explored the adjuvant use of hydroxycitric acid (HCA) to facilitate extracorporeal shock wave lithotripsy. They enrolled 81 patients in a randomised trial 1:1 comparing HCA with placebo. The 40 patients randomised to the HCA arm received one sachet of FagolitosPlus every 12 h 4 weeks prior to ESWL and one sachet daily for 6 weeks after ESWL. Treatment compliance was 88% in the experimental group and 95% in the control group. Patients with stones greater than 200 mm^2 and less than 150 mm^2 were excluded as well as all patients receiving medicines likely to produce of inhibit stone formation. The primary outcome metric was the intensity of fragmentation. All patients that took the HCA supplement had some fragmentation, while 17% of the patients on placebo did not have any fragmentation. The authors recommend the use of hydroxycitric acid prior to shock wave lithotripsy to improve stone fragmentation.

Garcia MCC, Cobos RC, Bohorquez AV et al. A randomized, double-blind, placebo-controlled trial of the use of hydroxycitric acid adjuvant to shock wave lithotripsy therapy in patients with calcium stones. Stone fragmentation results. Urolithiasis 2023; https://doi.org/10.1007/s00240-023-01456-0.

Platelet rich plasma for erectile dysfunction

Masterson et al. explored the role of platelet rich plasma (PRP) for the treatment of erectile dysfunction. Platelet rich plasma is currently being marketed for the treatment of sports injuries, facial aging, hair loss and erectile dysfunction. The authors recruited 61 men for the study: 28 received two treatments one month apart and 33 received placebo. Complete results were available from 24 men on treatment and 28 on placebo after one month and from 20 men on treatment and 24 on placebo after six months. The primary metric was the Minimally Clinically Important Difference in IIEF-EF score. Among men receiving the PRP, the IIEF-EF changed from 17.4 to 21 and among men receiving placebo the IIEF-EF changed from 18.6 to 21.6. There was no clinically significant difference between the two groups.

Masterson TA, Molina M, Ledesma B et al. Platelet Rich Plasma for the treatment of erectile dysfunction: A prospective, randomized, double-blind, placebo-controlled clinical trial. J Urol 2023; 210: 154–161.

Increased renal pressure in a porcine model

Finally, Lildal et al. from Denmark reported increased intrarenal backflow associated with increased renal pressure in a porcine model. They injected a Gadolinium saline solution into the renal pelvis of five pigs while occluding the ureteral pelvic junction with a balloon with a pressure monitor. They maintained a steady intrarenal pressure of 10, 20, 30, 40 and 50 mmHG. MRI of the kidneys was performed every 5 min. The MRI showed backflow into the kidney cortex in all cases. Visual damage was first seen after 15 min at a pressure of 21 mmHG. On the final MRI image, two thirds of the kidney cortex had intrarenal backflow at a pressure of 43 mmgHg for a mean duration of 70 min. The authors conclude that intrarenal backflow occurs earlier and at lower pressures than most clinicians realize.

Lildal SK, Hansen ESS, Laustsen C et al. Gadolinium enhanced MRI visualizing backflow at increasing intra-renal pressure in a porcine model. Plos One 2023; https://doi.org/10.1371/journal.pone.0281676.

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